Alberta Health Services Pharmacy Services

Issue 2 – April 2014, Updated February 2019

Antimicrobial Stewardship Backgrounder

Carbapenem Conundrum

Carbapenems are broad spectrum antibacterials which should be reserved for serious polymicrobial infections and infections with suspected or documented drug resistant organisms.

Appropriate stewardship of these important, often last resort, antibacterials is critical:

- While empiric use of carbapenems is appropriate in serious polymicrobial infections, or infections where there is a high likelihood of resistant organisms, tailoring to narrower spectrum agents based on culture and susceptibility results is crucial in order to avoid antibiotic overuse, potential resistance, and excessive cost.
- Use meropenem instead of imipenem, except for infections due to *Nocardia spp* or nontuberculous *Mycobacteria spp*., due to its lower cost.
- Ertapenem should not be used solely for its dosing convenience, even in the outpatient setting as alternatives are available, e.g. cefazolin + probenecid, or ceftriaxone 2g IV daily for simple cellulitis (+ metronidazole 500mg PO bid for polymicrobial infections).

Which Carbapenem to Use – ertapenem, imipenem, meropenem?

Spectrum of activity:
Carbapenems have broad spectrum activity against:

- Gram positive pathogens,
- Gram negative pathogens including extended-spectrum β-lactamase (ESBL)- and AmpC/inducible β-lactamase-producing Enterobacteriaceae, and
- anaerobes.

Did you know…
that **ertapenem** does NOT have activity against *Enterococcus spp*, *Pseudomonas spp*, or *Acinetobacter spp*?

In general, imipenem and meropenem have very similar spectra of activity, whereas ertapenem is more suitable for severe polymicrobial infections where *Enterococcus spp*, *Pseudomonas spp*, and *Acinetobacter spp* are not suspected, such as those acquired in the community.

Carbapenems do NOT have activity against methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus faecium*, *Stenotrophomonas maltophilia*, or atypical organisms (*Chlamydia/Chlamydophila spp*, *Legionella spp*, *Mycoplasma spp*). See Bugs & Drugs, Antimicrobial Spectrum of Activity for further details.

AHS clinical guidelines/Place in therapy:

ERTAPENEM
1. Empiric therapy of polymicrobial complicated skin and skin structure infections, including bite wound infections
2. Therapy of infections due to Enterobacteriaceae producing inducible (AmpC) β -lactamases or extended-spectrum β-lactamases (ESBLs) where there is resistance to first line agents and documented susceptibility to ertapenem
3. Empiric therapy for patients at high risk (e.g. previous ESBL infection, international travel history) of infections due to Enterobacteriaceae producing ESBLs
4. Therapy of community-acquired intra-abdominal infections in patients intolerant or unresponsive to first line therapy (ceftriaxone + metronidazole)

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IMIPENEM & MEROPENEM
Guidelines listed apply to both drugs unless otherwise indicated.
1. Therapy of severe infections involving Gram negative organisms in patients who are intolerant of, or unresponsive to, or whose isolates are suspected or documented to be resistant (e.g. ESBL, inducible (AmpC) ß-lactamases) to, first line agents and piperacillin-tazobactam (**meropenem preferred as less expensive than imipenem**)
2. Therapy of severe suspected or documented polymicrobial infections in patients who are intolerant of, or unresponsive to, or whose isolates are suspected or documented to be resistant to, first line agents and piperacillin-tazobactam (**meropenem preferred as less expensive than imipenem**. Some suggest imipenem preferred if Gram positive cocci in chains are predominant on Gram stain and *Enterococcus faecalis* is a probable pathogen, or *Enterococcus faecalis* is proven by culture, based on its vitro activity; however there are no clinical data suggesting differential response.)
3. Therapy of infections involving multi-drug resistant *Pseudomonas aeruginosa* where there is documented susceptibility to meropenem (**MEROPENEM**).
4. Empiric therapy in high risk febrile neutropenic patients +/- aminoglycoside (**meropenem preferred as less expensive than imipenem**).
5. Empiric therapy of post-traumatic/post-neurosurgical meningitis in combination with vancomycin (**MEROPENEM**)
6. Alternative to ceftazidime for therapy of central nervous system (CNS) infections due to *P. aeruginosa* (**MEROPENEM**)
7. As part of combination therapy of infections with *Nocardia spp* or nontuberculous *Mycobacteria spp* (**IMIPENEM**)

Dosage and relative cost:

Carbapenem	Usual Adult Dosage	Drug cost per patient/day relative to meropenem
Meropenem	500 mg IV q6h	1
Imipenem	500mg IV q6h	2.3
Ertapenem	1g IV daily	3.5

Did you know…
that **meropenem** is less than half the cost of imipenem and should be used instead (except for infections due to *Nocardia spp* or nontuberculous *Mycobacteria spp*)?

The following therapeutic interchanges for imipenem to meropenem and meropenem dosage are approved in AHS:

Original Order	Therapeutic Interchange
Imipenem in adults	Meropenem* in adults EXCEPT for: • Nocardia infections • nontuberculous Mycobacteria spp For these infections, imipenem is preferred. * Meropenem dosage: 500 mg IV q6h EXCEPT in cystic fibrosis, central nervous system infections, or ophthalmologic infections**
Meropenem 1-2 g IV q6-8h in adults	Meropenem 500 mg IV q6h EXCEPT in cystic fibrosis, central nervous system infections, or ophthalmologic infections**
** For these infections, contact prescriber to suggest dose of 2g IV q8h (adjust for renal dysfunction as per Bugs & Drugs).	

References

1. Baldwin CM, Lyseng-Williamson KA, Keam SJ. Meropenem: a review of its use in the treatment of serious bacterial infections. Drugs 2008;68:803-38.
2. Keating GM, Perry CM. Ertapenem: a review of its use in the treatment of bacterial infections. Drugs 2005;65:2151-78.
3. Rodloff AC, Goldstein EJC, Torres A. Two decades of imipenem therapy. *J Antimicrob Chemother* 2006;58:916-29.

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